Round Table

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Introduction

L. Pahlman. *Univ. Hospital Uppsala, Dept. of Surgery, Uppsala, Sweden*

The main treatment option in rectal cancer has for many years been surgery. Very little focus has been addressed to quality in surgery of rectal cancer. During the last twenty years several reports have been focused on surgical technique and nowadays most surgeons are aware of the technical aspects and total mesorectal excision has become the gold standard. With this more precise type of surgery where the anatomical planes are followed, local recurrence rate can be as low as less than 10%. Given that surgery is appropriate, one can discuss the value of adjuvant radiotherapy. Therefore, meticulous staging of the patients is necessary and the adjuvant treatment should be tailored to suite all different types of patients. The type of radiotherapy as well as the concomitant use of chemotherapy is under discussion. Moreover, the use of adjuvant chemotherapy has also been questioned. All studies using both radiotherapy and chemotherapy have been done during the period when surgery was not optimised. Very little data do support the use of chemotherapy, provided surgery is optimised. Therefore, this topic is still under the debate and should be further studied.

Summary: The round table discussion will focus on the results on good surgery, the place for radiotherapy provided surgery is optimised and discuss the role of chemotherapy to patients with rectal cancer.

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Is there a role for chemotherapy in the adjuvant treatment of rectal cancer?

E. Van Cutsem, K. Haustermans. *U.Z. Gasthuisberg, Internal Medicine, Leuven, Belgium*

Radiation and chemotherapy, when used alone in the adjuvant treatment of rectal cancer, have failed to prolong survival in most studies. Combined modality treatment seems attractive in order to reduce the rate of recurrence both at the primary tumor site and outside the pelvis and hence to improve survival.

It has been shown in the USA that a combined chemoradiotherapy is superior to postoperative radiotherapy alone. It has also been shown that a protracted infusion of 5-FU is superior to bolus injections of 5-FU/FA when combined with postoperative radiotherapy. In Europe, however, almost all experts favor the use of preoperative radiotherapy. It has been shown that preoperative irradiation decreases the risk of recurrence and improves overall survival, even if an optimal type of surgery (TME) is performed. These studies, however, have used the "short" irradiation regimen (5 x 5 Gy). Other experts favor the "long"regimen of irradiation (45 - 50 Gy; 1.8 Gy/Fraction). This "long" regimen has the advantage of downstaging the tumor and facilitating the resection, offering a greater chance to the patient of performing sphincter saving surgery compared to the "short" regimen. Therefore the challenge is to demonstrate that the addition of chemotherapy can further improve the results by increasing the rate of downstaging and thus offering a greater chance of complete resection and of sphincter saving surgery in low lying rectal cancers. The approach of combined preoperative chemoradiotherapy might also offer the hope of improving the survival by further decreasing the local recurrence rate and decreasing the occurrence of distant metastases.

Several studies are still ongoing to prove this concept: the EORTC and FFCD are randomizing patients between a preoperative radiotherapy (45 Gy) +/- chemotherapy (5-FU/LV). In this study patients are also randomized after the operation between adjuvant chemotherapy and no chemotherapy. A German study is randomizing patients with resectable rectal cancer between preoperative and postoperative chemoradiotherapy. Several phase 1 and 2 studies have shown the feasibility and the promising activity of combination studies of new drugs (irinotecan, oxaliplatin, capecitabine, UFT, raltitrexed) with radiotherapy in rectal cancer. The aim of these studies as well as the studies with new biological agents is to improve the effect of a combined chemo- and radiotherapy.

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Do we need adjuvant treatment if surgery is optimal in rectal cancer?

Bill Heald. *The Pelican Centre, Basingstoke, UK*

For 20 years complete prospective records have been kept of all rectal cancer cases handled by the unit. During the 80's there was no adjuvant therapy given to rectal cancer cases with the occasional exception of long course radiotherapy (RT) to those considered too fixed to be operable. During the mid 90's a policy of selective RT was introduced and during the year 2000 a visiting surgeon from Canada investigated the efficacy of this policy. The usual clinical criteria of fixation or tethering of the cancer was gradually being refined as the new potential of fine slice MRI was becoming appreciated. The advantages of this technology will be discussed.

Dr Simonovicz investigated 150 consecutive rectal cancers referred for surgery between 1994 and 1998 inclusive. 35 of these patients were selected for RT and in 115 cases no RT was deemed necessary. Of the 35, 19 underwent long course RT with the objective of reducing size and easing the operative difficulties involved in great fixity or as a consequence of tumour size. 16 patients underwent short course RT, mostly because of concern about one or other tumour margin. In some this related to the lowness of the cancer and its proximity to the dentate line and in others it related to the MRI evidence that a mesorectal margin was very close to the tumour. This is a particular problem with low anterior cancers in the male.

9 Local Recurrences (LR) (150 patients all stages)
3 out of 115 had no RT (LR 2.5%)
6 out of 35 underwent RT (LR 17.5%)
Overall LR rate 6%

For cancers of all stages with or without metastases at the time of presentation.

The key point that this small series illustrates is that a combination of clinical judgement and fine slice MRI is able to identify a group of patients that had NO RT, but whose LR rate from surgery alone was only 2.5%. There were no exclusions for age, fixation or inoperability, thus very satisfactory LR rates could be achieved in 3/4 of the patients without any adjuvant treatment at all provided a careful TME is performed.

It is clear that the problem cases could all be detected by these methods and that the 17.5%LR in those undergoing pre-operative RT embraces the great majority in patients where local control is going to be a problem. The value of adding chemotherapy to the pre-operative RT will be discussed. No patients underwent post-operative RT. Less than 20% had post-operative chemotherapy because this accorded with the patients' wishes.

It is concluded that the routine use of preoperative RT for all cases of rectal cancer was not an acceptable or justifiable policy, but that there should be a sea change towards SELECTIVITY FOR EACH FORM OF THERAPY.

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Do we need adjuvant treatment if surgery is optimal in rectal cancer?

J.W.H. Leer, E. Kapiteijn, C.A.M. Marijnen, I.D. Nagtegaal, C.J.H. van de Velde. *For the Dutch Colorectal Cancer Group, The Netherlands*

In the Dutch Colorectal Cancer Study which accrued 1861 patients between January 1996 and January 2000, patients were randomized either or not to receive 5 × 5 Gy preoperative radiotherapy (RT) followed by a total mesorectal excision (TME). The 2 year local recurrence rate was 8.5% in the TME alone group and 2.9% in the RT-TME group. Details of this study were recently published in the NEJM. Although the improved surgical procedure already led to a substantial reduction of the local recurrence rate, it was demonstrated that radiotherapy was still able to reduce the local recurrence rate significantly. The results of this trial however raise a few new questions.

Firstly, we have to decide whether the magnitude of this reduction is outweighed by the proportion of unnecessarily irradiated patients. To answer

this question we have to balance the burden of a local recurrence and the toxicity, especially late toxicity, of an irradiation given in vain. Secondly, we have to discuss whether before treatment we will be able to identify more precisely those patients likely or not to benefit from the treatment.

These questions will be discussed during the round table discussions.

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Autografting for acute myelocytic leukemia (AML) in Europe

N.C. Gorin[1], M. Labopin[2], L. Fouillard[1,2], E. Polge[2], F. Frassoni[3]. *On Behalf of the Acute Leukemia Working Party (ALWP) of EBMT, [1] Hospital Saint Antoine, Dept of Hematology, Paris, France; [2] EBMT, ALWP, Paris, France; [3] Ospedale San Martino, Hematology, Genova, Italy*

As of November 2000, the EBMT Registry contained information on 12447 patients with AML treated according to various schemes, all including HSCT. We restricted our analysis to the 10972 patients transplanted after January 1987.

1. Transplants in first remission (CR1): 8739 patients, consisting of 7348 adults and 1369 children. Of the adult patients, 3674 received an autograft (2337 Bone marrow of which 302 were purged in vitro and 1337 Peripheral Blood); 3674 received an allograft (3375 genoidentical, 91 family mismatches, 109 matched unrelated donors, 99 other). Of the children, 609 received an autograft (493 Bone marrow of which 140 were purged in vitro and 116 Peripheral Blood); 760 received an allograft (656 genoidentical, 32 family mismatches, 42 matched unrelated donors, 30 other).

2. Transplants in second remission (CR2): 2233 patients, consisting of 1837 adults and 388 children. Of the adult patients, 925 received an autograft (703 Bone marrow of which 151 were purged in vitro and 222 Peripheral Blood); 912 received an allograft (652 genoidentical, 68 family mismatches, 166 matched unrelated donors, 26 other). Of the children, 188 received an autograft (165 Bone marrow of which 42 were purged in vitro and 23 Peripheral Blood); 200 received an allograft (97genoidentical, 23 family mismatches, 72 matched unrelated donors, 8 other).

Overall results at five years will be presented: Results of ASCT have significantly improved after January 1994 (median date of the study), with marrow in CR1 and CR2 (LFS: 52±2% vs 48±1%, p=0.05, in CR1; LFS: 39±4% vs 33±2%, p=0.04 in CR2) and with PBSC in CR1 (LFS: 48±2% vs 42±4%, p= 0.05) in relation with a decrease in the relapse incidence.

3. New approaches for autografting: New developments include aggressive in vivo purging (first high dose consolidation), followed by autografting (second high dose intensification), combination of stem cells from bone marrow and from blood, both purged by mafosfamide, to constitute the graft, and tumor vaccination post transplant. Finally the sequential use of the high dose tumoricidal activity of autografting and the GVL effect provided by non myelo-ablative allogeneic stem cell transplantation is an option still to be investigated.

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Autologous transplantation in CML

Abstract not received.

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Allogeneic stem cell transplantation for patients with myelodysplastic syndromes and leukemias following MDS

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Most patients with myelodysplastic syndromes (MDS) are too old to be considered for intensive treatment such as stem cell transplantation (SCT). Allogeneic SCT from an HLA-identical sibling donor is the curative treatment option for a relatively young patient (younger than 60 years) with myelodysplastic syndrome or acute myeloid leukemia following a preceding phase of MDS. Age and lack of sibling donors limit this application. Alternative stem cell sources have been used more recently, such as unrelated donors, nonidentical family members or autologous transplants.

Most patients may benefit optimally from an allogeneic SCT when the transplant is performed as soon as an HLA-identical family member has been identified. Progression to more advanced leukemia conditions will be associated with a higher failure rate due to an increased relapse rate after SCT and a higher treatment-related mortality. Delay of the transplant may be justified in a minority of patients with refractory anemia or refractory anemia with ringsideroblasts without profound cytopenias or complex cytogenetic abnormalities, and no need for erythrocyte transfusions.

The present data from patients transplanted with sources of hematopoietic stem cells other than histocompatible sibling donors give an indication of the potentials of other forms of transplantation. The DFS of patients transplanted with histocompatible sibling donors was significantly better than the outcome of patients transplanted with other sources of stem cells. About one third of the patients transplanted with stem cells from histocompatible siblings and about one quarter of the patients with stem cells from other sources may be free of disease for three years or longer. The results of these treatment forms have improved considerably, but the continuing high treatment-related mortality warrants that these patients should be treated within investigational protocols.

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Autologous transplantation in lymphoma

Abstract not received.

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Autologous transplantation in myeloma

Abstract not received.